CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

***Letter from Alan Trounson, President of CIRM***

**November 24, 2010**

**Re: SCNT Workshop**

In the past few years, we have experienced scientific revolutions in the field of regenerative medicine. Human stem cell lines are being derived and differentiated into multiple cell and tissue types, which is helping us understand the normal processes underlying development and tissue formation. Cell culture models of diseases are being developed with human cells, which are already yielding interesting information about disease processes and could lead to much lower failure rates for drugs. Finally, several studies are evaluating stem cells and their derivatives for their therapeutic value in cell transplant and tissue regeneration applications. Stem cell biology is on the verge of changing the face of medicine.

One of the more exciting applications offered by human stem cells is the potential for advancing customized medicine. Stem cells derived from human patients allow the study of diseases in the context of an individual's genetic background. Cells derived from these stem cells offer the possibility of transplanting cells or tissues without the need for costly and debilitating suppression of the immune system. In spite of the exciting possibilities, the technology for deriving patient-specific cells is still in its infancy and far from optimal. Researchers and policymakers are still struggling to understand the scientific, ethical, and medical issues involved in generating and using customized stem cells.

The concept of customized stem cell therapies was first envisioned after scientists derived embryonic stem cells from mouse cells generated by somatic cell nuclear transfer (SCNT). In this technology, the genetic information in an egg is replaced with the nucleus of another cell. The resulting cell is totipotent and carries the genetic information of the donor cell nucleus – in other words, it is a stem cell that shares the genetic identity of a chosen individual. The creation of these cells created the field of customized stem cell therapy.

SCNT technology has been used to clone animals from a host of different species, from farm animals like cows and sheep to endangered species such as the gaur. SCNT has even been used to produce human blastocysts. However, SCNT is inefficient and requires large numbers of mature human oocytes that are not readily available. Because of the scarcity of human oocytes and the lack of any alternative to date, SCNT has never led to the production of human embryonic stem cells, which would be the essential starting material for developing customized, patient-specific cells and therapies. In the meantime, human stem cells have been derived by infecting adult skin cells with viruses carrying a panel of specific transcription factors. Although these cells, called induced pluripotent stem cells (iPSCs), are not therapeutic options at the moment because this involves insertional mutagenesis, they present a route for deriving customized cells that does not involve the need for human oocytes. In light of the rapid developments of iPSC and direct reprogramming using other specific transcription factors that short circuits the need for pluripotency, researchers are re-evaluating the need for human SCNT in developing patient-specific stem cells.

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CIRM's mission is to fund research that will advance the use of human stem cells for the treatment and cure of human disease. To understand the role of SCNT in furthering the development of human therapy, the organization partnered with the MRC to organize a Human SCNT workshop. The premiere researchers in this field were invited to discuss the progress and scientific impact of their research. Given the ethical and funding restrictions on human SCNT research, they were asked to identify the most important variables impacting progress in the field.

The workshop was a tremendous success in terms of summarizing the status of human SCNT and identifying the main research focus of the field with respect to alternative methods for producing human stem cells. This document is a report of the discussions that occurred at this meeting, supplemented by a brief review of SCNT and its relationship to broader issues in stem cell research. It will serve to inform our funding priorities in this area. CIRM is funding several basic biological studies that address the underlying need to identify a source of oocyte reprogramming factors. It is recommended that we continue to explore the fundamental mechanisms of reprogramming, including zebrafish and frog models. There was also strong support for continuing human SCNT research, despite the scarcity of donated human oocytes. As one way to address that scarcity, the UK and the state of New York have reconsidered prior prohibitions on donor compensation. CIRM is unable to pursue that approach, but it remains desirable for the key human SCNT researchers to examine ways that they could collaborate. CIRM and its collaborative funding partners may be able to assist by co-funding appropriate projects.

CIRM wishes to thank the MRC for their support of the SCNT Workshop and Lord Patel for acting as the Chair of the Workshop. The speakers were excellent and the discussion provided an extraordinary clarity to the issues that were explored. Every one of the speakers provided interesting data that was the source of much debate and discussion. From the basic amphibian research presented by John Gurdon that provided the basis of cellular reprogramming, to the discussions of the relative merit of iPSC and SCNT, this was a wonderful meeting and I thank every one of the Workshop participants.

I want to thank my colleagues, Uta Grieshammer, Geoff Lomax and Meybel Cortez, as well as Rob Buckle and the staff of the MRC for all their efforts to organize the Workshop, and Asha Nigh, with help from Uta Grieshammer, Kelly Shepard and Geoff Lomax, for writing the report.

Sincerely,

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